

Interaction of Alkylmercuric Compounds with Sodium Selenite. I. Metabolism of Ethylmercuric Chloride Administered Alone and in Combination with Sodium Selenite in Rats

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The effect of sodium selenite administered intragastrically in repeated doses to rats receiving ethylmercuric chloride po in various repeated doses (0.25 or 2.5 mg Hg/kg) on the excretion, whole-body retention, and organ distribution of mercury was studied.

Selenium was found to affect the distribution of ethylmercury among tissues and subcellular fractions of the kidneys and liver as well as its binding to proteins of soluble fractions in these organs.

Similarities and differences between the effect of interaction of sodium selenite with ethylmercuric chloride and methylmercury as well as inorganic mercury are also discussed.

Introduction

Employment of alkylmercury compounds, especially methylmercurials, in agriculture has resulted in several epidemic intoxications of humans (1-4). Ethylmercuric compounds are believed to be generally less toxic due to more rapid clearance (5, 6). However, these compounds have been used for a long time not only in agriculture (1, 7) but also as antiseptics, among others for preservation of blood plasma (8).

Numerous poisonings by ethylmercurials have been noted, however, in humans (9-13) and in animals (14, 15). However, available data on the toxicity, distribution, and metabolism of ethylmercurials, constituting a potential danger to living organisms, are scarce and generally fragmentary,

and concern mainly single-dose experiments (5, 10, 16-21). On the other hand, for estimation of chronic toxicity of alkylmercury compounds, of primary importance is the extent of their accumulation in the body, determined by the magnitude and duration of exposure, uptake rate, biotransformation efficiency and excretion rate.

Moreover, in the last decade considerable information has been gained on the detoxifying role of sodium selenite in experimental poisoning of animals with mercuric chloride (22-28) and methylmercury (28-35).

According to some authors, in the case of mercuric chloride the mechanism of the detoxifying action of selenium involves a decrease in the renal level of mercury, and therefore a diminution of the nephrotoxic effect (22, 24, 29, 36), the effect of selenite depending on its concentration as well as on the time and kind of exposure (37-42).

Results of studies on the mechanism of protective action of selenium in poisoning by methylmercury

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compounds are equivocal and sometimes contradictory (27, 43). No analogous data are available for ethylmercurials.

This study deals with metabolism of ethylmercuric chloride given rats according to two different schedules, alone or in combination with sodium selenite. The scope of the investigations covered excretion, tissue and organ retention, distribution in subcellular fractions of liver and kidneys, as well as binding to soluble-fraction proteins in these organs after repeated administration of the above compounds to animals.

Material and Methods

The experiments were performed on female Wistar rats weighing 150-200 g, fed standard LSM diet, and allowed to drink tap water *ad libitum*. The animals were divided into four groups of six rats each. Rats of groups I and II were given ethylmercuric chloride (EtHg; K and K Laboratories Inc., Plainview, N.Y. USA) in 0.1% sodium carbonate (Na_2CO_3 , POCh, Gliwice, Poland) through an intragastrical probe every other day for 14 days. The animals received 0.25 or 2.5 mg Hg/kg body weight, respectively, per single dose, labeled with ^{203}Hg ($\text{C}_2\text{H}_5^{203}\text{HgCl}$, Radiochemical Centre, Amersham, Bucks., England), 67.2 $\mu\text{Ci}/\text{mg}$. Animals of parallel groups Ia and IIa received ethylmercuric chloride in the same way and, separately, aqueous solution of sodium selenite (Na_2SeO_4 ; POCh, Gliwice, Poland), also intragastrically, 0.5 mg Se/kg per single dose. Depending on the body weight, the animals received 0.38-0.50 cm^3 of solutions of the above compounds every time.

At 24 hr after administration of the last dose of ethylmercuric chloride, rats were sacrificed under ether narcosis by heart puncture and then appropriate organs and tissues were removed.

Mercury was estimated directly by a radiochemical method from measurement of gamma-radiation in a USB-2 scintillation counter with a NaI/Tl crystal. The time of measurement was 100 sec.

Liver and kidneys were fractionated at a temperature of 0-4°C. The organs were homogenized in 7 volumes of 0.25M sucrose + 0.01% NaOH (pH 7.0) in a glass homogenizer (44). The homogenates were filtered through a gauze and centrifuged twice at 600g for 15 min to sediment the nuclear fraction (N). The postnuclear supernatant was centrifuged twice at 7000g for 15 min to sediment the mitochondrial fraction (M). The postmitochondrial supernatant was centrifuged once at 12,000g for 10 min. The sediment contained heavy lysosomes (L_h). The supernatant was centrifuged at 29,000g for 10 min to yield the sediment of light lysosomes (L_1). The

remaining supernatant was centrifuged at 144,000g for 1 hr. The obtained sediment contained microsomes (P), and the supernatant corresponded to the soluble fraction (S) which was then subjected to Sephadex G-75 chromatography in order to separate mercury-binding proteins. The chromatographic column, 2.5 × 60 cm, was eluted with formate buffer, pH 8.0. The elution rate was 10 cm^3/hr ; 3 cm^3 fractions were collected. The column was calibrated with: Dextran Blue (MW 2,000,000), cytochrome c (MW 12,700) and potassium chromate (MW 194). In the eluates mercury concentration was estimated as described previously, and protein concentration was monitored by absorbance measurements at 280 and 250 nm by using a VSU-2P spectrophotometer.

In the homogenates and individual subcellular fractions of liver and kidneys, protein was determined by the method of Lowry et al. (45).

All determinations were made separately for each animal.

Results

Throughout the experiment, the amount of ^{203}Hg excreted with feces and urine was monitored daily in rats exposed to different doses of $\text{C}_2\text{H}_5^{203}\text{HgCl}$ alone (groups I and II) or in combination with sodium selenite groups Ia and IIa (Figs. 1 and 2). Cumulative excretion of mercury in feces and urine during the 2-week exposure in animals of group I (0.25 mg Hg/kg) and group II (2.5 mg Hg/kg) was 36% (Fig. 3) and 26% (Fig. 4), respectively, of the administered dose.

A tenfold excess of selenium (group Ia) decreased the cumulative ^{203}Hg excretion from 36% to about 28% (Fig. 3). Selenium affected only urinary excretion of mercury, not the fecal excretion. This effect was visible in the course of both daily and cumulative excretion (Fig. 1).

An equimolar dose of selenium (group IIa) did not affect the excretion of mercury in the rats as compared with the group exposed only to ethylmercuric chloride (Figs. 2 and 4).

Retention of mercury in individual tissues and organs was also studied as a function of the dose of ethylmercuric chloride and the presence or absence of selenium. The contribution of individual tissues to the retention of ethylmercuric chloride is shown as a percentage of the cumulative dose in Figures 3 and 4. In rats of group I (Fig. 3) receiving the lower dose of ethylmercuric chloride (0.25 mg Hg/kg), retention was 64%. The metal was most concentrated in the kidneys, which retained 21% of the mercury administered. Blood as well as muscles and bones played an important role in the accumu-

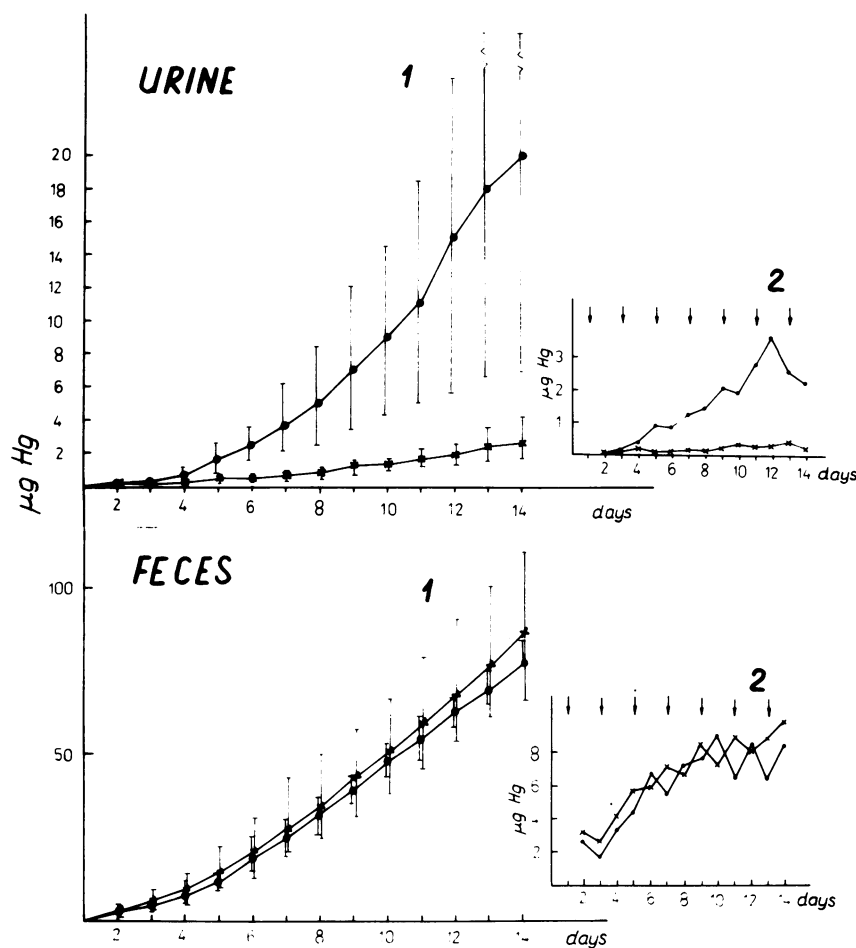


FIGURE 1. Cumulative (1) and daily (2) excretion of Et^{203}Hg in urine and feces during 2-week exposure of rats to $\text{Et}^{203}\text{HgCl} \pm \text{Se}$: (●) group I (0.25 mg Hg/kg), (×) group Ia (0.25 mg Hg/kg + Se). Bars represent range from six animals.

lation of the compounds studied, each retaining 17% of the total mercury given. Liver, intestines, and skin contained about 5% each, and the content of mercury in the remaining tissues did not exceed 1% of the cumulative dose. Brain had the lowest amount of the accumulated mercury (0.19% of the metal administered).

The mercury contents in the tissues of rats exposed to the low dose of ethylmercuric chloride (0.25 mg Hg/kg) are shown in Figure 5. The lowest content of this metal (below or about 1 $\mu\text{g Hg/g}$ tissue) was found for brain, muscle, and bones. For spleen and liver, the content of this metal did not exceed 3 $\mu\text{g/g}$ tissue, and for blood it was 6 $\mu\text{g/m}^3$. On the other hand, the renal content of mercury was higher by an order of magnitude, amounting to about 60 $\mu\text{g/g}$ tissue.

Administration of excess selenium (group Ia) resulted in similar changes in the tissue levels (Fig.

5) as in per cent contributions (Fig. 3) of the respective organs to the retention of $\text{Et}^{203}\text{HgCl}$, i.e., it considerably increased the level of mercury in brain (from about 0.39 to about 1.37 $\mu\text{g Hg/g}$ tissue), stomach (from about 1.45 to about 5.42 $\mu\text{g Hg/g}$ tissue), and liver (from about 2.6 to about 3.7 $\mu\text{g Hg/g}$) and decreased it in kidneys (from 56.9 to about 13.9 $\mu\text{g Hg/g}$) and blood (from 6.16 to about 4.55 $\mu\text{g Hg/m}^3$).

A tenfold higher dose of mercury (2.5 mg Hg/kg) resulted (Fig. 4) in an increased retention of mercury as compared with group I. The contributions of individual organs to the accumulation of mercury was similar to that observed in group I except that of kidneys, which was considerably lower (4.3%), and that of blood, which was higher (23%). The mercury in blood (Table 1) was almost completely bound by formed elements (99%).

Administration of a tenfold higher dose of mer-

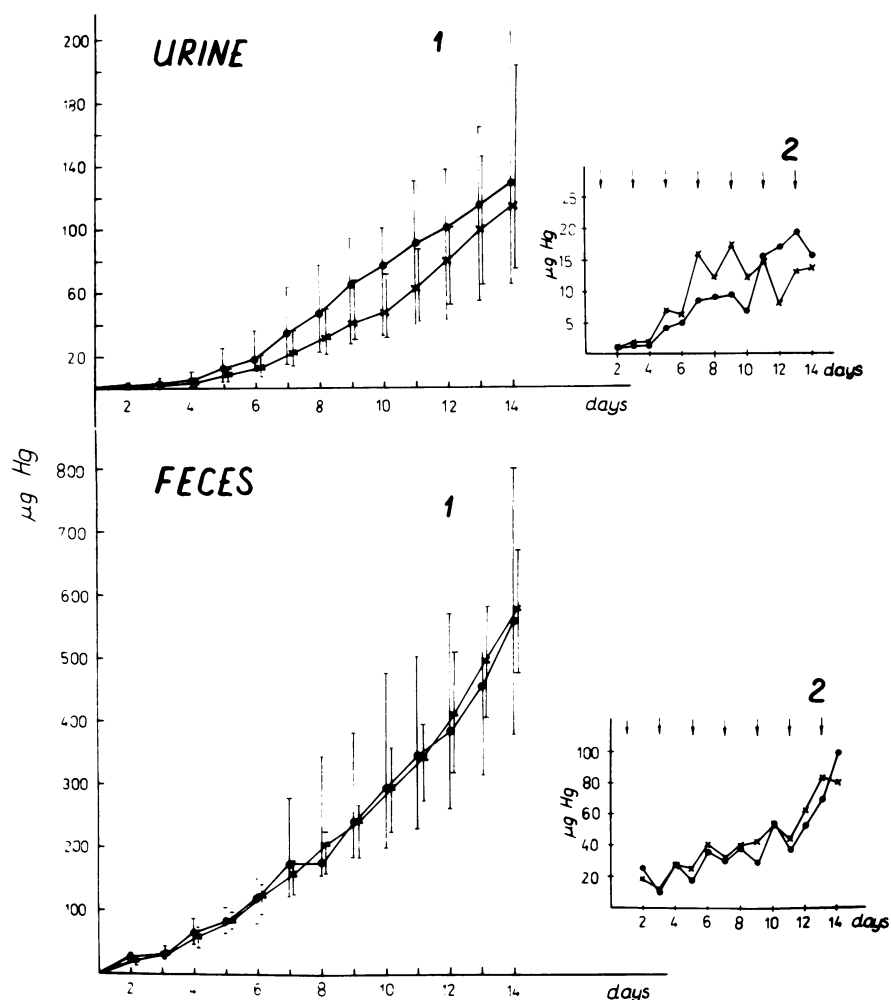


FIGURE 2. Cumulative (1) and daily (2) excretion of Et^{203}Hg in urine and feces during 2-week exposure of rats to $\text{Et}^{203}\text{HgCl} \pm \text{Se}$: (●) group II (2.5 mg Hg/kg), (×) group IIa (2.5 mg Hg/kg + Se). Bars represent range from six animals.

cury to rats (2.5 mg Hg/kg) resulted in a proportional, tenfold increase of its content in respective tissues, except for the kidneys where the mercury content increased as high as twentyfold in comparison with the group given a lower dose of ethylmercuric chloride (Fig. 5).

An equimolar dose of selenium with respect to mercury (group IIa) did not affect the Et^{203}Hg retention (Fig. 4) but altered its distribution in the body. As in group Ia, selenium increased the mercury contributions of liver, stomach, intestines and brain. Simultaneously, the contribution of kidneys to the retention of mercury increased considerably (from about 4.3 in group II to about 9.5% in group IIa).

An equimolar dose of selenium (group IIa) induced significant changes only in some rat tissues

(Fig. 6). As in the case of an excess of selenium (group Ia), an equimolar dose of this element with respect to mercury decreased the concentration of the mercury in blood (from 110 to about 59 $\mu\text{g Hg}/\text{cm}^3$) increasing it simultaneously in brain (from about 0.26 to about 0.57 $\mu\text{g Hg}/\text{g tissue}$). However, this dose of selenium had a different effect on the content of ^{203}Hg in kidneys which increased (from about 92 $\mu\text{g}/\text{g}$ in group II to about 213 $\mu\text{g}/\text{g}$ in group IIa).

Results from these experiments indicate that the molar ratio of mercury and selenium has a significant influence on the retention of mercury in tissues and organs of rats given ethylmercuric chloride. A tenfold excess of selenium increased the whole-body retention of mercury from about 64% in group I up to about 72% in group Ia (Fig. 3) and induced

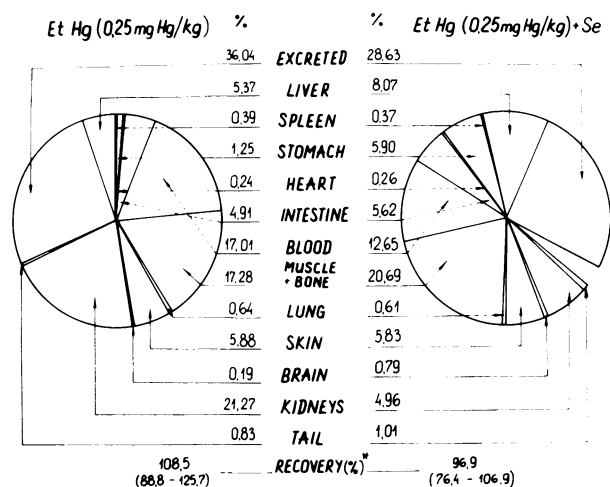


FIGURE 3. Tissue distribution of Et^{203}Hg (expressed as percent of cumulative dose) after 2-week exposure to $\text{Et}^{203}\text{HgCl} \pm \text{Se}$ for groups I (0.25 mg Hg/kg) and Ia (0.25 mg Hg/kg + Se).

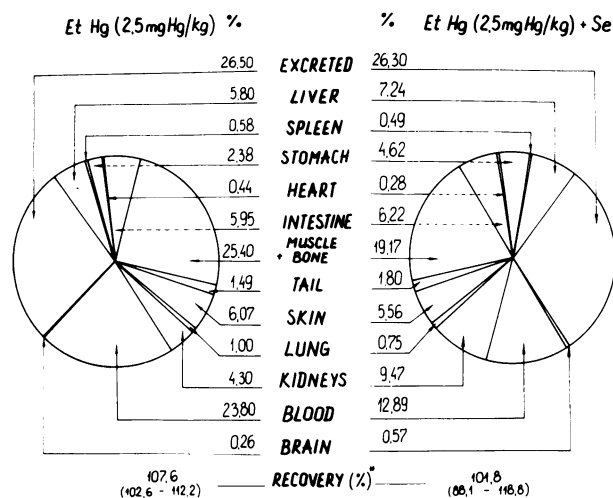


FIGURE 4. Tissue distribution of Et^{203}Hg (expressed as percent of cumulative dose) after 2-week exposure to $\text{Et}^{203}\text{HgCl} \pm \text{Se}$ for groups II (2.5 mg Hg/kg) and IIa (2.5 mg Hg/kg + Se).

changes in the organ distribution of mercury (Fig. 5). The concentration of mercury in kidneys decreased significantly (from 21% to 4%) while that in liver, stomach, intestines, muscles, and bones as well as brain increased. This refers especially to the brain which accumulated about 4-fold more mercury in this group (Fig. 3).

The content of ^{203}Hg /mg protein in subcellular fractions of rat kidneys and liver as a function of dose of ethylmercuric chloride and the presence sodium selenite is shown in Tables 2 and 3.

In animals of group I (Table 2) the level of mercury in individual subcellular fractions of the

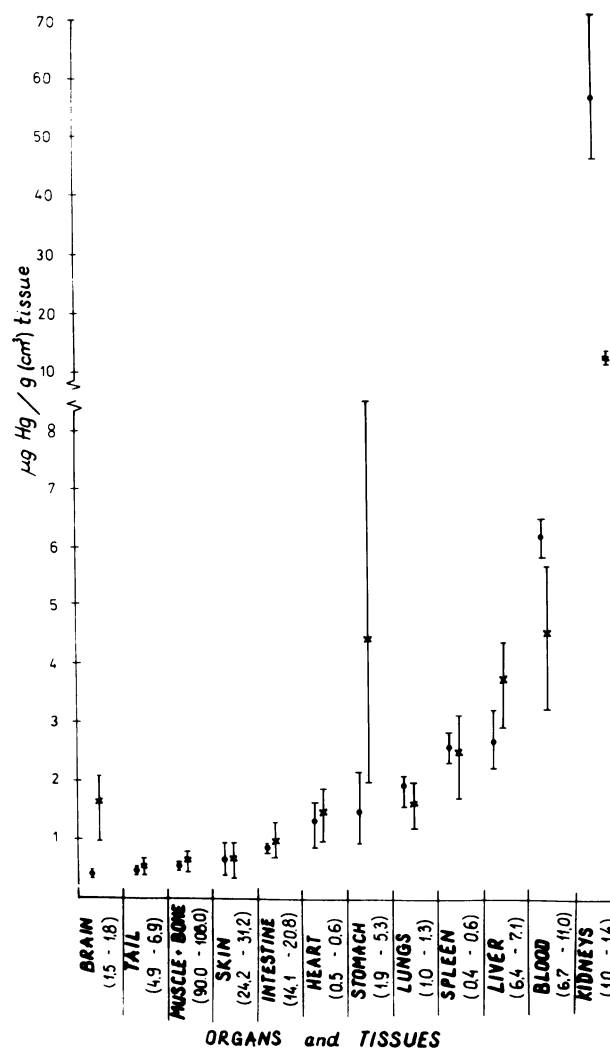


FIGURE 5. Content of Et^{203}Hg in rat tissue after 2-week exposure to $\text{Et}^{203}\text{HgCl} \pm \text{Se}$ (means and range from six animals): (●) group I 0.25 mg Hg/kg; (×) group Ia (0.25 mg Hg/kg + Se). Organ weight (g) and total blood volume (cm^3) indicated in parentheses.

Table 1. Contribution of plasma to ethylmercury accumulation after 2-week exposure of rats to $\text{Et}^{203}\text{HgCl} \pm \text{Se}$ (mean and range from 6 animals).

Group	Treatment	Et^{203}Hg in blood plasma, %
Group I	0.25 mgHg/kg	1.38
Group Ia	0.25 mgHg/kg + Se	1.23-1.55
Group II	2.5 mgHg/kg	1.64
Group IIa	2.5 mgHg/kg + Se	0.97
		0.74-1.09
		0.95
		0.86-1.06

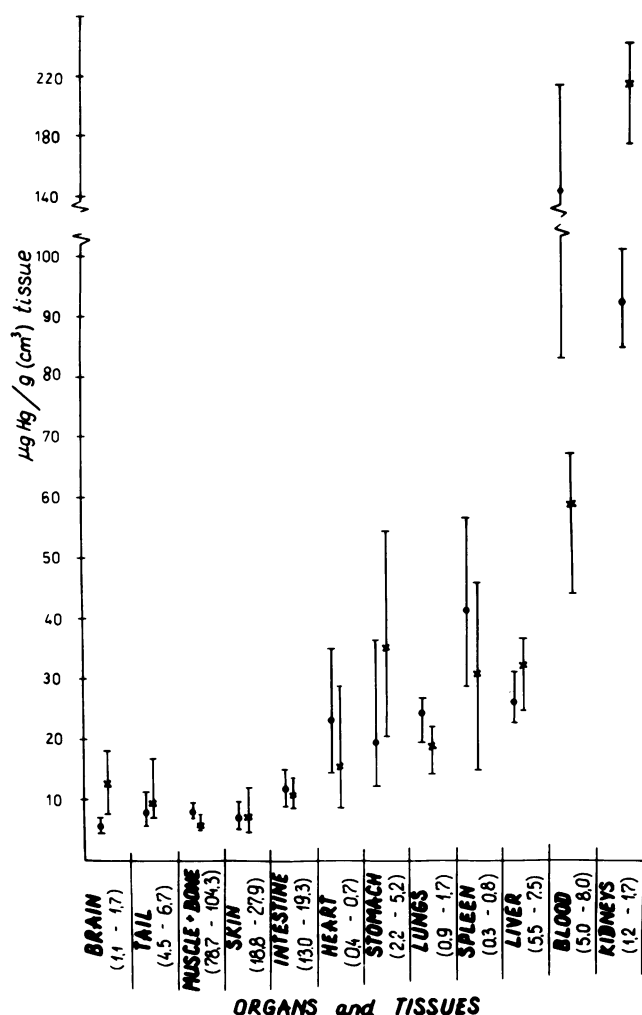


FIGURE 6. Content of Et^{203}Hg in rat tissues after 2-week exposure to $\text{Et}^{203}\text{HgCl} \pm \text{Se}$ (means and range from six animals): (●) group II (2.5 mg Hg/kg); (×) group IIa (2.5 mg Hg/kg + Se). Organ weight (g) and total blood volume (cm^3) indicated in parentheses.

liver ranged from about 0.008 (light lysosomes) to about 0.020 $\mu\text{g Hg/mg}$ protein (membranes, soluble fraction and microsomes).

The higher dose of mercury (group II) which induces a tenfold increase in the mercury content of this tissue (Fig. 5) led to a roughly equal increase in the concentrations of this metal in hepatic organelles. An exception was the microsomal fraction, where the increase was about twentyfold.

Sodium selenite in the liver of rats receiving a lower dose of mercury (group Ia) tended to increase the ^{203}Hg content of all fractions, but differences were minimal.

An equimolar dose of selenium with respect to

mercury (group IIa) induced an increase of ^{203}Hg concentration in mitochondrial and lisosomal fractions. Simultaneously, a decrease of mercury content in microsomal and soluble fractions was observed.

In the soluble fraction of liver, mercury was bound by high molecular weight proteins (Fig. 7), and the amount of the metal present in the peak corresponding to these proteins was dependent on the concentration of mercury in the total of the soluble fraction.

Sodium selenite did not affect the binding of ethylmercury in this fraction of the liver, irrespective of the dose.

For kidneys of rats of group I (Table 3), the level of mercury in individual subcellular fractions ranged from 0.182 (light lysosomes) to 0.681 $\mu\text{g Hg/mg}$ protein (soluble fraction).

The higher dose of ethylmercuric chloride (group II) which increased the level of mercury in this tissue twofold (Fig. 6) also elevated the mercury content of the subcellular fractions, as compared with group I. Exceptions were the nuclear, mitochondrial, and heavy lysosomal fractions where no changes were found in the content of this metal as compared with Group I (Table 3).

Administration of excess selenium with respect to mercury (group Ia) which decreased the level of mercury in the kidneys (Fig. 5) decreased its concentrations in individual fractions. The highest, about a tenfold decrease, took place in the soluble fraction (from about 0.681 to about 0.079 $\mu\text{g Hg/mg}$ of protein).

On the other hand, an equimolar dose of selenium (group IIa), which enhanced the mercury content of the kidneys (Fig. 6), increased similarly its levels in the organelles. The greatest increases were observed for the microsomal fraction (from about 0.616 to 5.109 $\mu\text{g Hg/mg}$ protein). An exception was the soluble fraction, where no changes were found in the content of this metal as compared with group II (Table 3).

The binding pattern of ^{203}Hg to the soluble-fraction proteins of kidneys of rats exposed to ethylmercuric chloride given in different doses alone or in combination with sodium selenite is shown in Figure 8.

In animals exposed to 0.25 mg Hg/kg, about 65% of the mercury present in the soluble fraction was bound to proteins of molecular weight of about 10,000, i.e., metallothionein-like proteins (Fig. 8). High molecular weight proteins bound about 17.60 and 18.05% mercury, respectively, depending on the molecular weight.

In the case of a high dose of mercury (2.5 mg/kg), metallothionein-like proteins dominated in the bind-

Table 2. Ethylmercury in subcellular fractions of rat liver after 2-week exposure to Et²⁰³HgCl with or without sodium selenite (mean and range from 4 animals).

Subcellular fractions	Et ²⁰³ Hg, µg/mg protein			
	Group I (0.25 mg Hg/kg)	Group Ia (0.25 mg Hg/kg + Se)	Group II (2.5 mg Hg/kg)	Group IIa (2.5 mg Hg/kg + Se)
H	0.014	0.019	0.146	0.489
M _s	0.012–0.017	0.014–0.030	0.139–0.159	0.137–0.548
	0.024	0.035	0.140	0.144
N	0.008–0.062	0.018–0.060	0.126–0.153	0.128–0.177
	0.010	0.019	0.154	0.160
M	0.006–0.012	0.010–0.035	0.054–0.275	0.116–0.246
	0.016	0.012	0.086	0.187
L _h	0.008–0.022	0.009–0.015	0.067–0.106	0.104–0.299
	0.012	0.012	0.083	0.181
L _l	0.008–0.015	0.008–0.014	0.054–0.113	0.150–0.224
	0.008	0.012	0.115	0.320
P	0.006–0.011	0.008–0.017	0.082–0.147	0.085–0.572
	0.021	0.026	0.469	0.217
S	0.018–0.023	0.019–0.035	0.305–0.633	0.167–0.296
	0.022	0.017	0.234	0.178
	0.016–0.032	0.012–0.020	0.187–0.267	0.164–0.189

Table 3. Ethylmercury in subcellular fractions of rat kidneys after 2-week exposure to Et²⁰³HgCl with or without sodium selenite (mean and range from 4 animals).

Subcellular fractions	Et ²⁰³ Hg, µg/mg protein			
	Group I (0.25 mg Hg/kg)	Group Ia (0.25 mg Hg/kg + Se)	Group II (2.5 mg Hg/kg)	Group IIa (2.5 mg Hg/kg + Se)
H	0.311	0.081	0.472	1.105
M _s	0.287–0.357	0.067–0.102	0.426–0.498	0.812–1.309
	0.232	0.109	0.340	0.725
N	0.148–0.345	0.096–0.118	0.272–0.409	0.329–0.940
	0.202	0.108	0.205	1.854
M	0.183–0.226	0.032–0.257	0.109–0.309	1.655–2.039
	0.370	0.046	0.353	1.941
L _n	0.280–0.479	0.032–0.069	0.353–0.353	1.013–2.415
	0.424	0.107	0.439	1.169
L _l	0.359–0.488	0.055–0.158	0.402–0.482	0.976–1.356
	0.182	0.060	2.547	1.074
P	0.171–0.194	0.059–0.060	1.800–4.361	0.532–1.505
	0.429	0.223	0.616	5.109
S	0.169–0.690	0.223–0.223	0.508–0.706	2.127–8.159
	0.681	0.079	0.716	0.810
	0.521–1.010	0.073–0.082	0.668–0.776	0.661–0.926

ing too, containing ca. 46% of the metal present in the soluble fractions of the kidneys (Table 4).

Sodium selenite, when administered in a tenfold excess with respect to mercury, did not displace the latter completely from low molecular weight proteins. It did cause a decrease in the mercury content of individual peaks, probably due to the diminution of the total mercury content of the kidneys (Fig. 5), especially of the soluble fraction (Table 3), but the distribution of this metal between the peaks remained relatively unchanged (Table 4).

The percentage of total mercury bound to low molecular weight proteins still contained about 50% of the total mercury present in the soluble fraction.

After administration of an equimolar dose of selenium with respect to mercury (group IIa) only slight changes were observed, indicative of a small decrease in the contribution of low molecular weight proteins in the binding of mercury (from 46.35% in group II to 34.8% in group IIa) in favor of high molecular weight proteins. However, the amount of this metal bound by protein classes of different

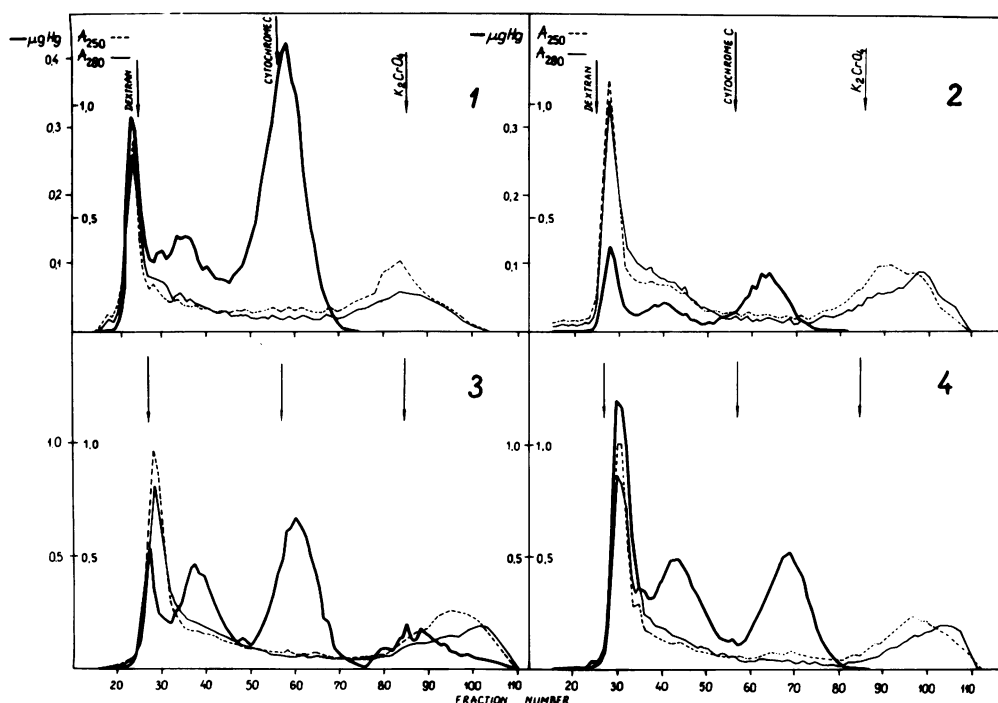


FIGURE 7. Separations of soluble fraction of rat liver after 2-week exposure to $\text{Et}^{203}\text{HgCl} \pm \text{Se}$: (1) group I (0.25 mg Hg/kg); (2) group Ia (0.25 mg Hg/kg + Se); (3) group II (2.5 mg Hg/kg), (4) group IIa (2.5 mg Hg/kg + Se). Sephadex G-75 column eluted with buffer as described in Methods. The curves correspond to (—) A_{280} , (---) A_{250} , and (—•—) $\mu\text{g}^{203}\text{Hg}$. Arrows indicate the position of Dextran Blue, Cytochrome c, and K_2CrO_4 .

molecular weight did not change significantly (Table 4), probably due to the unchanged total mercury content of the soluble fraction.

Discussion

The results presented here indicate that the processes of uptake, redistribution, and excretion of ethylmercuric chloride in the rat follow a pattern similar to that of methylmercuric chloride. However, its high accumulation in kidneys resembles the *in vivo* behavior of inorganic mercury.

This work indicates a high retention of ethylmercuric chloride in rats under conditions of chronic exposure, ranging from 64 to 74% after administration of doses differing by an order of magnitude. This retention was 20% lower than retention of methylmercuric chloride administered in the same (46) or similar doses (47).

Ethylmercuric chloride, like methylmercuric chloride, is excreted mainly in feces. The ratio of the amount of mercury excreted in urine to that excreted in feces during two weeks was about 1:8 (Fig. 1) or 1:10 (Fig. 2), respectively, depending on the dose. Urinary excretion of mercury was higher

at lower and single doses (16, 17), being the ratios were 1:5 and 1:2, respectively.

Literature data on the metabolism of ethylmercuric chloride are scarce and fragmentary and concern mainly dynamics of ethylmercury decay only in certain tissues after single (6, 10, 16-18, 21) or repeated doses (48, 49). These data indicate that the kidneys were especially efficient in accumulation of mercury in the experimental animals. Moreover, a tendency was demonstrated for a progressive accumulation of this compound in rat (17) and mouse kidneys (10) with time after administration of a single dose. Our previous studies indicate that of different mercury compounds administered in rats (methylmercurycyananidine, ethyl- and phenylmercuric chloride, and mercuric chloride), the highest concentrations of mercury in the kidneys were found after administration of ethylmercuric chloride (50). However, contribution of kidneys to the retention of mercury decreased with repeated exposure and with increasing doses of ethylmercuric chloride (Figs. 3 and 4). This is probably due to a limited binding capacity of specific renal proteins for mercury.

Apart from the soluble fraction in the kidneys,

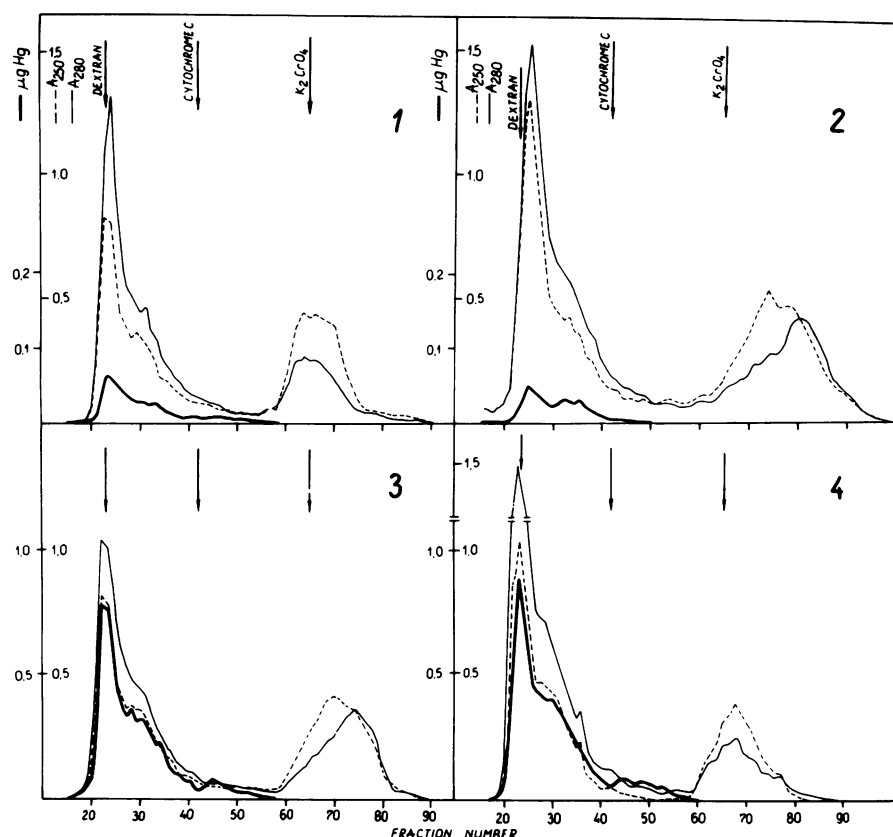


FIGURE 8. Separations of soluble fraction of rat kidneys after 2-week exposure to $\text{Et}^{203}\text{HgCl} \pm \text{Se}$: (1) group I (0.25 mg Hg/kg); (2) group Ia (0.25 mg Hg/kg + Se); (3) group II (2.5 mg Hg/kg); (4) group IIa (2.5 mg Hg/kg + Se). Sephadex G-75 column eluted with buffer as described in Methods. The curves correspond to (—) A_{280} , (---) A_{250} , and (—•—) $\mu\text{g}^{203}\text{Hg}$. Arrows indicate the position of Dextran Blue, Cytochrome c, and K_2CrO_4 .

Table 4. Content of ethylmercury in peaks of mercury-binding proteins of the soluble fraction of rat kidneys after 2-week exposure of rats to $\text{Et}^{203}\text{HgCl} \pm \text{Se}$; proteins separated by Sephadex G-75 chromatography.

Treatment	EtHg content, %			
	Peak 1	Peak 2	Peak 3	Peak 4
Group I (0.25 mg Hg/kg)	17.60	18.05	64.33	—
Group Ia (0.25 mg Hg/kg + Se)	21.18	22.60	50.30	—
Group II (2.5 mg Hg/kg)	14.60	29.80	46.35	9.25
Group IIa (2.5 mg Hg/kg + Se)	32.70	31.20	34.80	—

irrespective of the dose, other cellular organelles also played an important role in the accumulation of ethylmercury. In this respect ethylmercuric chloride behaved unlike inorganic mercury which was accumulated more efficiently in the soluble fraction of the kidneys, chiefly bound to metallothionein-like proteins (37, 40, 51-53).

On the other hand, it has been noticed previously (53) that ethylmercuric chloride, like HgCl_2 , in-

duces a statistically significant increase in the level of metallothionein-like proteins in kidneys of rats exposed chronically to this compound. It resulted from those studies, too, that irrespective of the dose of ethylmercuric chloride, mercury present in the soluble fraction of the kidneys was bound mainly to low molecular weight proteins (Fig. 8) and the contribution of these proteins was higher than after a single dose of this compound (5). Probably these proteins bind chiefly inorganic mercury released from ethylmercuric chloride by biodegradation, and this process is determined by magnitude of the dose (54).

It has been found, too, that at high doses of ethylmercury when the contribution of kidneys to the accumulation of mercury is decreased, that of blood is increased (Fig. 4). This efficient accumulation of ethylmercury in blood of experimental animals in combination with the slow atrophy of this tissue (10, 16, 17, 21) results in accumulation of mercury in brain, the organ believed to be critical in poisoning with alkylmercurials (2, 4, 55, 56).

It is noteworthy that the brain:blood mercury concentration ratio, calculated on the basis of total Et^{203}Hg concentration in these tissues of rats, is fairly constant at 0.01, irrespective of the dose of ethylmercury and of the kind of exposure.

In the case of interaction between ethylmercuric chloride and sodium selenite, the blood:brain mercury concentration ratio was observed to increase severalfold as compared with values obtained for animals exposed to ethylmercuric chloride alone.

The constant ratio of mercury concentrations in brain and blood indicates that the level of mercury in rat brain depends on its level in blood and can be calculated from the latter as in the case of methylmercury in humans. It should be emphasized on the basis of these observations that high doses of ethylmercury which could be deposited in kidneys only to a limited extent but which are progressively accumulated in blood constitute a potential danger of a sudden appearance of ethylmercury poisoning symptoms. Similar results have been observed for methylmercury (57).

A characteristic feature of interaction between HgCl_2 and sodium selenite administered in equimolar doses is an increase in the whole-body retention of mercury and a decrease in the levels of this metal in kidneys with concomitant increases in liver and blood (23, 40, 47, 58). This may be due to formation of stable complexes of these elements with proteins in liver and blood (38, 59, 60). Occurrence of complexes of this type have been demonstrated for other rat tissues (61).

In the case of ethylmercuric chloride, an equimolar dose of selenium not only did not decrease but even increased the mercury content of rat kidneys (Figs. 4 and 6). A small excess of selenium did not alter the level of mercury in this organ (50). The effect of diminution of the mercury level after exposure to ethylmercuric chloride was observed only after application of a tenfold selenium excess (Fig. 5).

Contrary to the interaction between HgCl_2 and sodium selenite, even a tenfold excess of the latter did not result in a shift of ethylmercury from low to high molecular weight proteins, inducing only a decrease in the concentrations of this metal in appropriate peaks (Fig. 8).

Similarity between ethylmercury and HgCl_2 in the interaction with selenium can be observed for the rat only in kidneys and exclusively for low doses of ethylmercury. It concerns probably only the inorganic mercury released from the alkyl linkage, as the process of biotransformation of low doses of ethylmercury in rats proceeds in kidneys with a high efficiency, both after single (10) and repeated exposure (50). This question is the subject of our further studies.

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